REMARKS

Reconsideration of the outstanding rejections is requested for the reasons set forth below.

Drawings

As an initial matter, it appears that the Examiner overlooked the replacement drawings that Applicants filed on October 30, 2003. The replacement drawing for Figure 1 includes the sequences for the variable portions of the light chain of the G-250 antibody with indications for the CDRs, and is fully supported by the disclosures in the priority PCT application and the two U.S. provisional applications. See Figure 1s in the priority applications.

Claim Rejections - Under 35 USC §112

Claims 1-10 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Examiner contended that claim 1 is vague and indefinite for reciting "a nucleotide sequence encoding the CDR3 region (designated H3), or/and encoding the CDR2 region (designated H2), or/and encoding the CDR1 region (designated H1), as shown in Fig. 1 or/and Fig. 6," and "at least one copy of a nucleic acid encoding the antigen-binding site of the light chain of an antibody comprising a nucleotide sequence encoding the CDR3 region (designated L3), or/and encoding CDR2 region (designated L2), or/and encoding the CDR1 region (designated L1), as shown in Fig. 1 or/and Fig. 6." The Examiner further noted that Fig. 6 consists of a light chain and a heavy chain amino acid sequences, but does not clearly indicate the CDR regions, and figure 1 consists of the amino acid sequence for the heavy chain variable region only, not a light chain variable region.

This rejection, as explained above, appears to stem from the Examiner overlooking the replacement drawings filed on October 30, 2003. Further, claim 1 as amended incorporates sequence identifiers for the CDRs in the claims. A substitute Sequence Listing is concurrently filed herewith. Thus, Applicants submit that the indefiniteness rejection has been overcome and the rejection should be withdrawn.

Claim 6 was rejected for reciting "substantially does not alter" on the ground that it is not clear as to what the phrase "substantially does not alter the amino acid sequence" means. The Examiner contended that it is not clear as to what physical or chemical properties are "not altered." The Examiner also contended that it is not clear as to what the word "alter" means. Insomuch as "substantially" is concerned, claim 6 as amended does not recite the term anymore. Insomuch as "alter" is concerned, it is submitted that claim 6 clearly recites that "the amino acid sequence of the antigen-binding site of the polypeptide to be expressed" is not altered, and the meaning of the term "alter" is so clear in the context that there is no ambiguity left in the claim as amended.

Claims 1-10 were rejected under 35 U.S.C. 112, first paragraph, as not being enabled. The Examiner's contented that antibodies as defined by the claims which may contain less than the full set of the six CDRs from the heavy and light chain variable regions are not likely to have the required binding function. It is submitted that claim 1 as amended requiring all of the six CDRs overcomes the rejection.

Claim Rejections - Under 35 USC §102

Claims 1-5 were rejected under 35 U.S.C. 102(b) as being anticipated by Weijtens et al. (The Journal of Immunology, 157:836-843, 1996). The Examiner interpreted the claims as being drawn to a vector producing monoclonal G250 antibody and a method of production of the antibody by introducing the recombinant vector system into a mammalian cell. The Examiner contended that Weijtens et al. teach eukaryotic cells (i.e., lymphocytes) derived from hybridoma cell DSM ACC 2526 obtained by transfer of the genetic material encoding the antigen-binding site (i.e., VH and VL) of the G250 antibody into the lymphocytes (i.e., receptor cell or cell derived from hybridoma DSM ACC 2526) which produce a single-chain antibody (i.e., scFv), particularly relying on pages 836-37 of the reference. The Examiner further contended that the product of claims 1-3 is defined in terms of a laboratory designation rather than by physical characteristics, structure or the process by which the product is prepared,

and consequently, comparison of this product with the prior art is difficult since the Office is not equipped to manufacture the claimed product and/or prior art products that appear to be related and conduct comparisons. Applicants traverse.

As an initial matter, Applicants point out that claims 1-3 as amended define the subject matter using amino acid sequences.

A reference must contain an enabling disclosure of the claimed subject matter in order to qualify as prior art under section 102(b). See MPEP §2121.01. Applicants submit that merely knowing that someone did it once does enable one skilled in the art to repeatedly reproduce it; merely describing that someone did it once does not provide enabling disclosure to repeatedly reproduce it.

Weijtens teaches that "[t]he genes encoding the V_H and the V_L domains of the G250 mouse mAb were isolated by anchored PCR(26) from cDNA prepared from G250 mAb-producing hybridoma cells ..." However, Weijtens does not disclose any sequence information of G250 or how to make the hybridoma cell (DSM ACC2526), which produces G250 monoclonal antibodies. All that Weijtens teaches is that someone did it.

Production of a hybridoma cell line producing G250 through an immunization procedure from scratch using prior art technique starting from a very unspecific immunogen, *i.e.* a cell homogenate of primary RCC lesions from unspecific patients, for example, as taught in Oosterwijk et al. (WO88/08854), is very difficult and its success is quite unpredictable. The immunogen, like that of Oosterwijk, comprises a multitude of antigenic determinants or epitopes which are capable of eliciting immune reactions in the experimental animal. Consequently, a variety of antibodies with different specificities would be produced. It is therefore highly unlikely that a hybridoma cell producing the G250 antibody would be consistently or repeatedly obtainable starting from scratch using prior art procedures, for example, like the one disclosed in Oosterwijk.

Moreover, the antigen recognized by the G250 antibody is not a linear epitope which can be specified by a defined amino acid sequence of the MN antigen, but is a non-linear conformational epitope of a still unknown tertiary structure. See example 2 and pages 8-11 of U.S. Utility Patent Application 10/470,940 (published as US2004-0077081), which describes the mapping of the epitope recognized by the monoclonal G250 antibody. It is evident from these data that the identification and isolation of the specific G250 epitope is exceedingly complicated due to the fact that no strong reactivity of partial sequences of the MN antigen with the monoclonal antibody G250 could be identified. Therefore, Applicants submit that one skilled in the art was not enabled to make or practice the claimed subject matter of the present Application. Thus, Weijtens is not an anticipatory reference and the rejection should be withdrawn.

Claims 1-5 were rejected under 35 U.S.C. 102(b) as being anticipated by Carceller et al. (U.S. Patent No. 5,969,107, issued: October 19, 1999). The Examiner interprets claim 1 as directed to any antibody consisting of any of the CDRs selected from figure 1 or figure 6 and contends that Carceller et al. teach an anti-idiotypic antibody compromising a CDR (H1 as shown in figure 1 of the instant application), and a vector system to produce such antibodies. In response, Applicants submit that claim 1 as amended overcomes the rejection.

Claim Rejections - Under 35 USC §103

Claims 1-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Oosterwijk et al. (a) (WO 88/08854, Published 11/17/1988) in view of Oosterwijk et al. (b) (Seminars in Oncology. 1995. 22(1):34-41) in view of Robinson et al. (U.S. Patent No. 5,618,920; issued 4/8/1997) and in view of Queen et al. (U.S. Patent No. 5,530,101; issued 6/25/1996). It appears that the Examiner contends that the existence of monoclonal G250 antibody was already known at the time of filing of the present Application, its use in the therapy of renal cell carcinoma was also known and one skilled in the art already had all the means to decipher the nucleic acid sequences of the V_H and V_L of G250 antibody, and therefore, one skilled in the art would have been able

to figure out the specific sequences recited in the claims of the present Application if one wished to do so. Applicants traverse.

Applicants submit that the reasoning of the Examiner is a typical example of obvious-to-try rationale, which is an incorrect obviousness standard. MPEP 2145, X, B. The correct obviousness standard is obviousness of the result and reasonable expectation of success. MPEP §2141, II.

There is no guidance in prior art leading one to the actual sequences, especially the CDR sequences. The prior art provides at best a possibility that one might be able to figure out the sequences if one wished so, but still leaves one completely in the dark as to what the actual sequences are i.e., the result of trying to sequence G250. The result is not obvious.

Moreover, as explained above, the mere knowledge of the existence of monoclonal G250 antibody or a hybridoma cell producing the antibody does not impart knowledge of how to obtain the antibody or the hybridoma cell from scratch. As explained above, the procedure taught in Oosterwijk for obtaining monoclonal G250 antibody is so unpredictable, one skilled in the art would probably have not been able to obtain monoclonal G250 antibody, which is the starting point of amino acid sequencing, without undue burden. As a result, there was no reasonable expectation of success for finding out what the sequences are at the time of filing of the present Application. Therefore, Applicants submit that the rejection is improper and should be withdrawn.

New claims

It is submitted that claim 11 is patentable for the reasons set forth above with regard to claim 1.

In view of the foregoing, it is submitted that the present application is now in condition for allowance. Reconsideration and allowance of the Application is requested. The Director is authorized to charge any fees or overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

By _____

Hyunkweon Ryu
Attorney for Applicants
Registration No. 58,283
ROTHWELL, FIGG, ERNST & MANBECK, P.C.
Suite 800, 1425 K Street, N.W.
Washington, D.C. 20005
Telephone: (202)783-6040
Facsimile: (202)783-6031

#1352419